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Klaus Pfizenmaier

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PILLSBURY WINTHROP SHAW PITTMAN LLP (CV)

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/594,189	Applicant(s) PFIZENMAIER ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 9/29/2011.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 28-32 and 34-50 is/are pending in the application.
- 5a) Of the above claim(s) 46 and 47 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 28-32, 34-45 and 48-50 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☒ Claim(s) 28-32 and 34-50 are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☒ The drawing(s) filed on 29 September 2011 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/20/11</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 29 September 2011 has been entered in full. Claims 1-28 are cancelled. Claims 28-32, 34-45 are amended. Claims 48-50 are added.

Claims 46 and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 May 2010.

Applicant's election of antibody fragment as the species of Component C in the reply filed on 17 May 2010 is also acknowledged.

Claims 28-32, 34-45 and 48-50 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to the declaration as set forth at page 3 of the previous Office Action (01 April 2011) is *withdrawn* in view of the new declaration submitted 29 September 2011.
2. The objection to the specification as set forth at pages 5-6 of the previous Office Action (01 April 2011) is *withdrawn* in view of the amended specification (29 September 2011).
3. The objections to claims 28-45 as set forth at page 6 of the previous Office Action (01 April 2011) are *withdrawn* in view of the amended and cancelled claims (29 September 2011).
4. The rejection of claims 28-45 under 35 U.S.C. 112, second paragraph as set forth at pages 6-9 of the previous Office Action (01 April 2011) are *withdrawn* in view of the amended claims (29 September 2011).
5. The rejection of claims 28-45 under 35 U.S.C. 112, first paragraph (lack of enablement) as set forth at pages 9-15 of the previous Office Action (01 April 2011) is *withdrawn in part* in

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view of the Wiese declaration filed under 37 CFR § 1.132 on 29 September 2011. The declaration and accompanying evidence indicate that a single chain tumor necrosis factor (scTNF), as generated in the instant specification, is immobilized to the surface of microporous beads and removes/depletes TNFR from serum.

Sequence Compliance

The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (29 September 2011) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (01 April 2011) are *withdrawn*.

Drawings

The replacement drawings were received on 29 September 2011. These drawings are acceptable.

Claim Objections

- 6. Claims 28-45 are objected to because of the following informalities:
 - 6a. In claim 28, line 1, the comma after the term "depletion" should be deleted.
 - 6b. In claim 43, line 2, after the term "wherein", the word "component" should be inserted.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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7. Claim 50 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 50 recites the limitation "antibody derivative" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claims 44, 43, and 38, from which claim 50 ultimately depends, do not recite the limitation "antibody derivative".

9. Claim 50 is rejected as being indefinite because in line 2, it is not clear if the phrase "or antibody fragment" is intending to further limit the antibody fragment or antibody derivative in line 1 or is intending to further limit the humanized antibody in line 2.

10. Claim 28 refers to "tumor necrosis factor receptor (TNFR)" in the preamble and the body of the claim. However, the specification discloses that there are two tumor necrosis factor receptors, TNFR1 and TNFR2, that the trimerized monomer of the invention may bind (page 33). The state of the art also teaches that there are numerous TNF receptor family members (see Idriss et al. Microsc Res Tech 50: 184-195; page 189, Table 2). Hence, it is not clear what TNFR is being removed or depleted from blood. Is it one TNFR in particular, or all?

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 28-32, 34-45 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for binding of the blood or the blood fractions expressing TNFR to a surface or particle coupled to a polypeptide wherein the polypeptide comprises at

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least three components A and at least two components B, wherein each component A comprises a tumor necrosis factor (TNF) monomer or a TNF extracellular domain fragment or variant thereof that binds TNFR1 and/or TNFR2, *does not reasonably provide enablement for* binding of the blood or the blood fractions expressing TNFR to a surface or particle coupled to a polypeptide wherein the polypeptide comprises at least three components A and at least two components B, wherein each component A comprises a tumor necrosis factor (TNF) monomer or a functional fragment or a functional derivative thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 28 is directed to a method for extracorporeal depletion, or removal of tumor necrosis factor receptor (TNFR) from blood or blood fractions comprising the following steps:

- (a) optional separation of the blood into one or more blood fractions with solid or liquid components;
- (b) binding of the blood or the blood fractions expressing TNFR to a surface or particle coupled to a polypeptide wherein the polypeptide comprises at least three components A and at least two components B, wherein each component A comprises a tumor necrosis factor (TNF) monomer or a functional fragment or a functional derivative thereof, and each component B is a peptide linker, under conditions allowing binding of TNFR in the blood or the blood fractions to the surface or the particle; and
- (c) separating TNFR from the blood or the blood fractions, thereby depleting or removing TNFR from the blood or blood fractions.

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Applicant's arguments (29 September 2011), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

At page 15 of the Response, Applicant asserts that Exhibit A shows data indicating the removal/depletion of TNFR from PBS and bovine serum using TNF monomers (scTNF), demonstrating that the scTNF was biologically active. Applicant argues that the specification discloses sequence of scTNF monomers (amino acids 79-181 of human TNF) in Figures 19, 20, 23, and 26 (page 49, line 17 to page 50, line 24; page 52, lines 7-23; page 54, lines 6-23). Applicant contends that given the declaration and Exhibit A and the disclosure of scTNF monomers in the specification, it would not require undue experimentation to make or use the claimed invention.

Applicant's arguments have been fully considered but are not found to be persuasive. According to the specification, scTNF-L_{short} (construct A-II) is composed of 3 TNF modules, each module comprising the extracellular domain of natural human TNF (amino acids 79-281) (see page 49, lines 17-30 through the top of page 50). The cys-scTNF-L_{short} construct (construct B-II), and scTNF construct (construct E) all contain 3 TNF modules of the extracellular domain of natural human TNF (amino acids 79-281) (see pages 50 and 52). Hence, the scTNF (aka, construct E) utilized in the declaration and Exhibit A submitted on 29 September 2011 contains 3 TNF modules of the extracellular domain of natural human TNF (amino acids 79-281). Each of the trimer constructs generated only use one TNF sequence, natural human TNF of amino acids 79-281. The specification, declaration, and Exhibit A do not generate a polypeptide comprising three components A, wherein each component A is a TNF monomer fragment or variant thereof.

As discussed in the previous Office Action of 01 April 2011, the specification of the instant application teaches that a polypeptide or a component A or a fragment or variant thereof

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is functional within the meaning of the invention, provided it exhibits its biological activity of function (page 6, lines 20-21). The specification discloses that "[i]n the case of functional fragments and the functional variants of the invention, these biological functions can in fact be changed, e.g., with respect to their specificity or selectivity, but with retention of the basic biological function" (page 6, lines 23-26). The specification teaches that the fragment of a monomer represents its extracellular domain, which corresponds to the entire extracellular domain of the soluble wild-type member of the TNF ligand family or a segment thereof (page 7, lines 12-24). The specification also teaches that "[i]n particular, monomers, polypeptide, or proteins, or fragments thereof that have sequence differences relative to the corresponding native sequences are designated as variants of biologically active monomers, polypeptides, or proteins, or fragments thereof, or a component A...These sequence deviations can be one or more insertion(s), deletion(s), and/or substitution(s) of amino acids, whereby there is a sequence homology of at least 60%, preferably 70%, more preferably 80%, also more preferably 85%, even more preferably 90%, and most preferably 97%" (page 8, lines 4-11). However, the specification does not enable all possible TNF ligand family monomer fragments and variants with a biological activity (as component A) other than the wild-type (non-mutated) extracellular domains of TNF ligand family members. The specification also does not teach any functional or structural characteristics of the monomer variants, fragments, and derivatives recited in the claims.

The claims of the instant application do not require the TNF monomer to have any particular structure or function, such as binding TNFR1 or TNFR2. This particular function is critical since the claimed method is depletion or removal of TNFR1 and/or TNFR2 from blood or blood fractions (via the mechanism of TNF binding to TNFR1 and TNFR2). Certain positions

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in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, *Biochemistry* 29:8509-8517; Ngo et al., 1994, *The Protein Folding Problem and Tertiary Structure Prediction*, pp. 492-495). However, Applicant has provided little or no guidance to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the TNF monomer segments which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. For instance, Idriss et al. teach that one TNF α mutant where Arg31 is substituted with Asp, shows preferentially reduced binding to TNFR2 (page 191, column 1, 2nd full paragraph). Idriss et al. state that another TNF α mutant, termed M3S, contains four different changes and exhibits 11- and 71-fold lower binding affinities for human TNFR1 and TNFR2 (page 191, column 1, 3rd full paragraph). Furthermore, the broad brush discussion of making and using fragments and variants in the specification does not constitute adequate guidance to practice the claimed method, but rather, constitutes an invitation to experiment empirically to determine how to practice the suggested method to obtain the results required by the claims.

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Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate the infinite number of TNF monomer fragments and variants recited in the claims and possibly screen same for activity; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and that biological activity cannot be predicted based on structural similarity; and the breadth of the claims which fail to recite any specific structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

12. Claims 28-32, 34-45 and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth for claims 28-45 at pages 15-18 of the previous Office Action of 01 April 2011.

Applicant's arguments (29 September 2011), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

At the bottom of page 16 of the Response, Applicant argues that in terms of functional scTNF comprising three identical TNF monomers (amino acids 79-281 of human TNF) in Figures 19, 20, 23, and 26. Applicant submits that further support for various species of TNF is found in the specification, for example, at page 56, line 13 to page 60, line 3 and Example 3 at

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pages 64, line 13 through page 65, line 7. Applicant argues that the specification teaches that the polypeptide or a fragment or variant thereof is functional within the meaning of the invention, provided it exhibits its biological activity of function. Applicant contends that the specification discloses that the biological activity may be changed with respect to specificity or selectivity, but with retention of the basic biological activity. Applicant argues that functional fragments and functional variants of TNF monomers would be known or ascertainable by the skilled artisan. Applicant concludes that in view of the specification, knowledge and skill in the art at the time of the invention, and functional fragments or functional variants of scTNF having the requisite activity, the claims are adequately described.

Applicant's arguments have been fully considered but are not found to be persuasive. According to the specification, scTNF-L_{short} (construct A-II) is composed of 3 TNF modules, each module comprising the extracellular domain of natural human TNF (amino acids 79-281) (see page 49, lines 17-30 through the top of page 50). The cys-scTNF-L_{short} construct (construct B-II), and scTNF construct (construct E) all contain 3 TNF modules of the extracellular domain of natural human TNF (amino acids 79-281) (see pages 50 and 52). Thus, each of the trimer constructs generated only use one TNF sequence, natural human TNF of amino acids 79-281. However, the claims of the instant application do not require that the TNF monomer functional fragment or functional variant possess any particular conserved structure or function. Thus, the claims are drawn to a genus of proteins and methods of using such.

The specification teaches that "[i]n the case of functional fragments and the functional variants of the invention, these biological functions can in fact be changed, e.g., with respect to their specificity or selectivity, but with retention of the basic biological function" (page 6, lines 23-26). The specification teaches that the fragment of a monomer represents its extracellular

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domain, which corresponds to the entire extracellular domain of the soluble wild-type member of the TNF ligand family or a segment thereof (page 7, lines 12-24). The specification also clearly teaches that "[i]n particular, monomers, polypeptide, or proteins, or fragments thereof that have sequence differences relative to the corresponding native sequences are designated as variants of biologically active monomers, polypeptides, or proteins, or fragments thereof, or a component A...These sequence deviations can be one or more insertion(s), deletion(s), and/or substitution(s) of amino acids, whereby there is a sequence homology of at least 60%, preferably 70%, more preferably 80%, also more preferably 85%, even more preferably 90%, and most preferably 97%" (page 8, lines 4-11).

In this case, the specification fails to disclose and there is no art-recognized correlation between the structure of the genus of functional fragments or functional variants of a TNF monomer and a function (i.e., binding TNFR1 and TNFR2). The specification does not teach which amino acids can vary from the full-length (wild-type) or extracellular domain of a TNF ligand family member and still result in a protein that retains a specific activity. Therefore, the description of full-length and extracellular domains of TNF (page 11, lines 12-27; page 49, Figure 19) is not adequate written description of an entire genus of functional fragments or functional variants of a TNF monomer. The skilled artisan cannot envision the detailed chemical structure of the protein fragments and variants of the encompassed claims and methods of using such, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. The broad brush discussion of making and screening for TNF monomer fragments and variants does not constitute a disclosure of a representative number of members. No such fragments or variants were made or shown to have activity. The specification's general discussion of making and using fragments and variants

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constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 28-32, 34, 36, 37, 39, 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lentz (WO 99/61085) and Klysner et al. (US 2003/0185845).

Lentz teaches an ultrapheresis method of removing compounds of less than 120,000 daltons molecular weight to stimulate a patient's immune system to attack solid tumors (page 2, lines 26-29). Lentz discloses that the method is useful for treatment of patients with cancer or other disorders characterized by elevated levels of TNF receptors (page 3, lines 28-31). Lentz

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discloses that the method is sufficient to filter at least one blood volume (page 2, lines 30-31 through page 3, line 1). Lentz teaches that the patient is pheresed to selectively remove soluble receptors, such as soluble tissue necrosis factor receptor-1 (sTNFR-1) or soluble tissue necrosis factor receptor-2 (sTNFR-2) (page 3, lines 2-7). Lentz continues to state that the sTNFR can be removed by binding to the cytokine or an epitope thereof of the receptor (page 3, lines 7-8; page 11, lines 6-23). Lentz teaches that the cytokine or epitope thereof can be immobilized in the filter, in a column, or using other standard techniques for binding reactions to remove proteins from the blood or plasma of a patient (page 3, lines 8-10). Lentz teaches that the treated blood and permeate may be returned to the patient (page 6, lines 19-28; page 7, lines 3-16; Figures 1-2).

Lentz does not teach that the cytokine is a polypeptide, wherein the polypeptide comprises at least three components A and at least two components B, wherein each component A comprises a TNF monomer and each component B is a peptide linker.

Klysner et al. teach that the cytokine, TNF α , binds two different TNF receptors, TNFR55 (TNFR1) and TNFR75 (TNFR2) (page 9, [0121]). Klysner et al. disclose a monomerized trimer construct comprising three TNF α regions, separated by either a tri-glycine linker or an epitope encoding region (page 20, Example 8; page 10 [0131-0136]). Klysner et al. teach that these monomerized trimers (i) have a conformation as close to the native TNF α as possible, (ii) bind receptors, (iii) are soluble, and (iv) are stable in the absence of detergents or other additives (page 10, [0133]; page 2, [0028]).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the apheresis method that selectively removes soluble TNFRs from blood via a cytokine that binds the receptors as taught by Lentz by utilizing the TNF α

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monomerized trimer construct as taught by Klysner et al. as the cytokine that binds the soluble TNFRs. The person of ordinary skill in the art would have been motivated to make that modification because the substitution of one known element for another yields predictable results (see *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007)).

Additionally, the TNF α monomerized trimer construct of Klysner et al. is stable and binds sTNFR1 and sTNFR2 (page 10, [0133]; page 2, [0028]). A person of ordinary skill has good reason to pursue known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense (see *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007)). The person of ordinary skill in the art reasonably would have expected success because similar apheresis methods were already being performed at the time the invention was made. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

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Conclusion

No claims are allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Lentz et al. Therapeutic Apheresis 3(1): 40-49, 1999 (review of soluble TNFR1 and TNFR2 and elevated levels in cancer; apheresis for cancer treatment)

Lentz et al. Jpn J Apheresis 16(1): 107-114, 1997 (therapeutic apheresis selectively removes a low molecular weight protein fraction from whole blood and results in breast cancer regression)

Howell et al. U.S. Patent 6,379,708 (teach removing TNFR1 and TNFR2 from blood using a binding partner, such as antibodies or TNF α /TNF β ; columns 6-7)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571)272-0881. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB

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30 November 2011

/Bridget E Bunner/
Primary Examiner, Art Unit 1647